【Grant-in-Aid for Scientific Research(S)】

Integrated Science and Innovative Science (Comprehensive fields)

Title of Project： Magnetic Resonance Molecular Microimaging

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Research Area：Neuroscience in General

Keyword：Clinical Neuroscience, Non-invasive Neuroimaging

【Purpose and Background of the Research】

There is no doubt that one of the most important aspects of life science research is its contribution to the clinical management of human disease processes. Rapid advancements in molecular biological techniques have provided hitherto unobtainable, powerful tools and given mankind great hope for effective treatment of degenerative brain diseases. At the same time, however, a critical problem has become apparent, namely, the lack of an effective *non-invasive*, quantitative imaging method for quantitative assessment of disease processes. The theoretical spatial resolution limit for magnetic resonance imaging (MRI) is 4μ. Therefore, a final goal of clinical MRI technologies is to provide an *in vivo* microscopic application, analogues to histo-pathological examination. To realize such a goal, in addition to achieving the ultimate spatial resolution, a molecular imaging method based on specific ligand similar to positron emission tomography (PET) needs to be developed. The current project is designed to develop such a imaging method utilizing O-17 labeled specific ligand and JJ Vicinal Coupling Proton Exchange (JJVCPE) technique.

【Research Methods】

In vivo molecular microimaging is indisputably the next generational imaging technique, which will significantly impact on clinical practice of central nervous system (CNS) diseases. Standard clinical technique for molecular imaging is PET. However, theoretical limit of spatial resolution of PET is 0.7 mm (700 μ), implying that microscopic application cannot be obtainable for PET. Currently, the only imaging technique capable of producing clinical microimaging is MRI.

In order to have ligand based molecular imaging in MRI, labeling of ligand with molecules, which can affect MRI contrast mechanisms, is essential. However, standard relaxation reagents, such as gadolinium, manganese, or iron, all possess strong charges and therefore, cannot cross the plasma membrane. Here, the proposed non radioactive, isotope of oxygen-17 plays an important role.

Under appropriate molecular structural settings, JJ vicinal coupling occurrs between O-17 and proton can be observed. Furthermore, in water solution, exchanges between O-17 coupled proton and proton of surrounding water molecule occurs. Accordingly, appropriately designed O-17 labeled materials can change apparent T2 relaxation of nearby water protons.

In this study, we will investigates two representative O-17 labeled materials, namely, water and Pittsburgh B Compound (PIB), which is originally developed as amyloid imaging ligand for PET.

【Expected Research Achievements and Scientific Significance】

The project is designed to develop MRI molecular imaging technique on ultra-high filed MRI system. The technique is robust. Nevertheless, its scientific significance can be easily appreciated by considering only one of the specific cases, i.e. amyloid microimaging. The technique is capable of detecting senile plaques (SPs) in preclinical stage of Alzheimer's disease (AD), leading to realistic prevention of AD. The obvious significant beneficial impact which this project will bring to clinical medicine needs no elaboration.

【Publications Relevant to the Project】

・Nakada T, Matsuzawa H, Igarashi H, Fujii Y, Kwee IL: *In vivo* visualization of senile plaque like pathology in Alzheimer's Disease patients by MR microscopy on a 7T system. J Neuroimag **18**:125-129, 2008.
・Nakada T, Matsuzawa H, Kwee IL: High Resolution Imaging with High and Ultra-High-Field MRI Systems. NeuroReport **19**:7-13, 2008.

【Term of Project】 FY2009-2013

【Budget Allocation】 164,400 Thousand Yen

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